Alerts, Notices, and Case Reports

Secondary Syphilis Presenting as Nephrotic Syndrome

GREGORY J. MAGARIAN, MD
CURTIS MARR, MD
Portland, Oregon

NEPHROTIC SYNDROME is characterized by an increase in glomerular capillary permeability to proteins, especially albumin, which ultimately leads to sufficient proteinuria to exceed hepatic synthetic replacement capacity. The resultant hypoalbuminemia and corresponding hypo-oncotic pressure lead to generalized edema formation.

The usual causes of the nephrotic syndrome include nonimmunologic glomerular damage, such as from diabetes mellitus and amyloidosis, and immunologic damage to glomeruli from such diseases as systemic lupus erythematosus, occult malignancy (including hematologic and solid tumors), medications (especially gold and penicillamine), primary renal glomerulonephropathies (minimal change disease, focal glomerulosclerosis, membranous nephropathy, and rapidly progressive glomerulonephropathy), and some infectious diseases, such as malaria and subacute bacterial endocarditis. Immune complexes within the glomeruli, identified by immunofluorescence, are characteristic of these disorders. In a recent review of manifestations of secondary syphilis in 854 patients, the nephrotic syndrome was not noted in any patient.[1] Because of the rarity of nephrotic syndrome from secondary or latent syphilis and the uncertainty of its clinical course with antisyphilitic therapy, we report a case of the acute onset of nephrotic syndrome in a middle-aged man whose clinical course and serologic status were observed closely for a year after treatment with penicillin.

Report of a Case

The patient, a 53-year-old man, was seen one week after he had developed generalized edema and a mildly pruritic maculopapular rash involving his trunk, face, arms, and palms beginning several days after what he thought was an upper respiratory tract viral syndrome. The edema formation was associated with a 9-kg (20-lb) weight gain during the same brief period. Other than increasing fatigue, he had no other complaints.

He had a 20-year history of diabetes mellitus. His blood glucose levels had been well controlled on insulin therapy with near-normal hemoglobin A_{1C} levels as well. Before this admission to hospital, he had recent normal blood urea nitrogen and creatinine levels although proteinuria (2+) was noted on a routine urinalysis two years previously. No quantification of his proteinuria was done at that time. He was unmarried, heterosexual, and said he had had no sexual encounters for at least three years before this illness. Before that, he claimed to have been monogamous sexually with his ex-wife.

On physical examination, his blood pressure was 154/70 mm of mercury with otherwise normal vital signs. He had obvious anasarca and a maculopapular, pink rash of well-demarcated spots about 5 to 10 mm in diameter covering his trunk, arms, and face and slightly involving his palms. There were no oral or genital lesions. His examination otherwise revealed no abnormalities, and he had no funduscopic change of diabetes or other end-organ stigmata of long-standing diabetes.

Pertinent laboratory data included a hematocrit of 0.39 (39%) and a hemoglobin level of 130 grams per liter (13.0 grams per dl). A leukocyte count was 7.9×10^9 per liter (7,900 per μl) with a normal differential. A blood urea nitrogen level was 4.3 mmol per liter (12 mg per dl), and a creatinine level was 80 μmol per liter (0.9 mg per dl). His serum albumin level was 20 grams per liter (2.0 grams per dl). Microscopic analysis of a urine specimen revealed an inactive sediment. On a 24-hour urine collection, he had 12.3 grams of protein with a normal creatinine clearance. A VDRL test was positive at 1:256. A fluorescent treponemal antibody (FTA) test was also strongly positive. Antinuclear antibodies were not found. A serum complement 3 level was 0.51 grams per liter (51 mg per dl) (normal 0.55 to 1.20). Human immunodeficiency virus antibody testing was negative. A skin biopsy of his rash revealed a heavy lymphohistiocytic perivascular inflammatory reaction, especially prominent in the superficial dermis but also to a lesser degree in the deeper dermis as well. This was reported as consistent with secondary syphilis.

The patient's acute clinical onset of nephrotic syndrome in association with his rash, skin biopsy histopathologic findings, and strongly positive VDRL and FTA was felt to represent classic secondary syphilis complicated by nephrotic syndrome, despite his persistent denials of risk factors for acquiring it. Although diabetic nephropathy was considered as a possible cause, because of the temporal relationship between the occurrence of classic manifestations of secondary syphilis and the acute onset of the nephrotic syndrome in this patient with serologic confirmation of syphilis, a renal biopsy was not considered justified, pending his response to antisyphilitic treatment, because other potentially reversible causes of the nephrotic syndrome were not found. He was treated with penicillin G benzathine, 2.4 million units intramuscularly, for secondary syphilis and furosemide, 40 mg per day, for his edema.

Three weeks later, his edema had resolved and he had minimal residual rash. The furosemide therapy was discontinued. Within another two weeks, his rash had disappeared, and he remained free of edema. His VDRL titer at that time had diminished to 1:64. A second dose of penicillin was given. Three months after treatment with penicillin was initiated, a 24-hour urine specimen showed a pronounced reduction in the urine protein level to 0.8 grams per 24 hours with a rise in the serum albumin level to 38 grams per liter. Five months after he received penicillin, his VDRL reacted only at a 1:1 dilution. Again, the temporal correlation of his clinical and serologic manifestations of secondary syphilis and

(Magarian GJ, Marr C: Secondary syphilis presenting as nephrotic syndrome. West J Med 1992 Jun; 156:654-655)

From the Section of General Medicine, Department of Veterans Affairs Medical Center (Dr Magarian), and the Department of Medicine, Oregon Health Sciences University (Drs Magarian and Marr), Portland.

response to treatment were felt to confirm the etiologic association between secondary syphilis and nephrotic syndrome and to exclude diabetic nephropathy as the cause of his nephrotic syndrome.

A year after the diagnosis of nephrotic syndrome from secondary syphilis was made, he continued to be free of edema. A lumbar puncture was done a year later to exclude neurosyphilis. Cerebrospinal fluid chemistry measurements and cell counts were normal, and the VDRL was negative.

Discussion

From 1981 to 1989, the incidence of primary and secondary syphilis increased 34% in the United States.[2] This increase has occurred since the mid-1980s and is a result of the remarkable increase in the incidence of syphilis among African Americans. Syphilis continues to be the great mimicker of diseases. Many of its later manifestations are related to immune complex formation with tissue deposition.[3-9] There are few reports of renal involvement from secondary or latent syphilis in the past two decades in the English-language literature.[7-14] In the cases in which biopsies were obtained, an immune complex glomerulonephritis has been identified.[7-10,14] Microscopic studies of renal biopsy specimens have most often revealed a membranous glomerulonephritis,[3,4,7,14] but minimal change[8,13] and proliferative glomerulonephritis[9] have also been identified. Antitreponemal antibody has been eluted from renal glomerular deposits obtained by biopsy.[3,9]

Together these case studies support an immune complex origin for the nephrotic syndrome associated with secondary or latent syphilis.[3-14] Fortunately, this nephrotic state is short-lived with appropriate antisyphilitic treatment. In our patient and the several others with reported follow-up, the nephrotic state appears to last from a week[8] to several months after appropriate antimicrobial therapy has been administered.[14] With an increasing incidence of primary and secondary syphilis occurring since the mid-1980s,[2] syphilis must be considered in a patient with otherwise unexplained nephrotic syndrome. Because of the association of the acquired immunodeficiency syndrome with syphilis, syphilis should be considered when unexplained proteinuria and nephrotic syndrome occur in such patients.

REFERENCES

1. Mindel A, Tovey SJ, Timmins DJ, Williams P: Primary and secondary syphilis, 20 years' experience—2. Clinical features. Genitourin Med 1989; 65:1-3

2. Rolfs RT, Nakashima AK: Epidemiology of primary and secondary syphilis in the United States, 1981 through 1989. JAMA 1990; 264:1432-1437

3. Gamble CN, Reardan JB: Immunopathogenesis of syphilitic glomerulonephritis: Elution of antitreponemal antibody from glomerular immune-complex deposits. N Engl J Med 1975; 292:449-454

4. O'Regan S, Fong JS, de Chadarévian JP, Rishikof JR, Drummond KN: Treponemal antigens in congenital and acquired syphilitic nephritis: Demonstration by immunofluorescence studies. Ann Intern Med 1976; 85:325-327

5. Jorizzo JL, McNeely MC, Baughn RE, Solomon AR, Cavallo T, Smith EB: Role of circulating immune complexes in human secondary syphilis. J Infect Dis 1986; 153:1014-1022

6. Baughn RE, McNeely MC, Jorizzo JL, Musher DM: Characterization of the antigenic determinants and host components in immune complexes from patients with secondary syphilis. J Immunol 1986; 136:1406-1414

7. Braunstein GD, Lewis EJ, Galvanek EG, Hamilton A, Bell WR: The nephrotic syndrome associated with secondary syphilis: An immune deposit disease. Am J Med 1970; 48:643-648

8. Sterzel RB, Krause PH, Zobl H, Kuhn K: Acute syphilitic nephrosis: A transient glomerular immunopathy. Clin Nephrol 1974; 2:164-168

9. Walker PD, Deeves EC, Sahba G, Wallin JD, O'Neill WM Jr: Rapidly progressive glomerulonephritis in a patient with syphilis: Identification of antitreponemal antibody and treponemal antigen in renal tissue. Am J Med 1984; 76:1106-1112

10. Bhorade MS, Carag HB, Lee HJ, Potter EV, Dunea G: Nephropathy of secondary syphilis: A clinical and pathological spectrum. JAMA 1971; 216:1159-1166

11. Hellier MD, Webster ADB, Eisinger AJM: Nephrotic syndrome: A complication of secondary syphilis. Br Med J 1971; 4:404-405

12. Bahl V, Obineche EN, Mistry CM: Nephrotic syndrome and secondary syphilis. E Afr Med J 1975; 52:172-175

13. Krane NK, Espenan P, Walker PD, Bergman SM, Wallin JD: Renal disease and syphilis: A report of nephrotic syndrome with minimal change disease. Am J Kidney Dis 1987; 9:176-179

14. Tang AL, Thin RNT, Croft DN: Nephrotic syndrome and hepatitis in early syphilis. Postgrad Med J 1989; 65:14-15

Seat Belt Use During Pregnancy

MELISSA SCHIFF, MD
TRACEY KASNIC, RNC
KAREN REIFF, RN
DOROTHY PATHAK, PhD
Albuquerque, New Mexico

MOTOR VEHICLE crashes are a major cause of death in women of childbearing age,[1] and a major proportion of all maternal deaths are caused by motor vehicle crashes.[2,3] It is well documented that the use of seat belts greatly reduces serious injury and death.[4-6] Several studies of pregnant women have shown improved survival of mothers and their fetuses when seat belts were worn at the time of motor vehicle crashes.[7,8] Although the use of seat belts has been mandated by state law in New Mexico since 1986, the percentage of pregnant women using seat belts is not known. Furthermore, little is known about attitudes and beliefs of pregnant women regarding the use of seat belts during pregnancy. The frequency of seat belt use and the factors influencing their use were investigated in women attending obstetric clinics affiliated with the University of New Mexico Department of Obstetrics and Gynecology.

Patients and Methods

During April and May 1989, all pregnant women receiving prenatal care through the University of New Mexico Hospital and its affiliated community clinics were asked to complete a questionnaire. All questionnaires were in English. Non-English-speaking patients, who make up about 5% of the clinic population, did not complete the questionnaire. The sample we analyzed thus represents a convenience sample of English-speaking, English-reading gravid women. The questionnaire was designed to be self-administered to assess demographics, risk-taking behavior—previous motor vehicle crashes, substance abuse—trimester of the initiation of prenatal care, seat belt use before and during pregnancy, reasons for seat belt use or nonuse, and personal knowledge about the use of seat belts during pregnancy. Data were analyzed using SAS packages (Version 5, SAS Institute, Cary, North Carolina). Statistical significance was evaluated using the χ^2 test unless otherwise indicated.[9]

Results

A total of 207 questionnaires were received from the two hospitals and from the four community-based obstetrics clinics. The response rate was approximately 75%. Most respondents were young, married, Hispanic gravid women (Table

(Schiff M, Kasnic T, Reiff K, Pathak D: Seat belt use during pregnancy. West J Med 1992 Jun; 156:655-657)

From the Department of Obstetrics and Gynecology (Dr Schiff, Ms Kasnic, and Ms Reiff) and the Department of Family, Community, and Emergency Medicine (Dr Pathak), University of New Mexico School of Medicine, Albuquerque.

Reprint requests to Melissa Schiff, MD, Department of Obstetrics and Gynecology, University of New Mexico Hospital, 2211 Lomas Blvd NE, Albuquerque, NM 87131-5286.